UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

ATHENA DIAGONISTICS, INC., ISIS INNOVATION LIMITED, and MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN e. V.,	*	
Plaintiffs,	*	
v.	*	Civil Action No: 15-cv-40075-IT
MAYO COLLABORATIVE SERVICES, LLC, d/b/a MAYO MEDICAL LABORATORIES, and MAYO CLINIC,	*	
Defendants.	*	

MEMORANDUM & ORDER

August 25, 2016

TALWANI, D.J.

Plaintiffs Athena Diagnostics, Inc., Isis Innovation Limited, and Max-Planck-Gesellschaft zur Forderung der Wissenschaften e.V., allege that two tests developed by Defendants Mayo Collaborative Services, LLC, and Mayo Clinic, infringe on Plaintiffs' patent, U.S. Patent No. 7,267,820 (" '820 Patent"). Third Am. Compl. ("Complaint") [#92]. Defendants move to dismiss Plaintiffs' complaint arguing that the '820 patent is invalid under 35 U.S.C. § 101 because the claimed method applies routine and conventional techniques to a law of nature. Defs.' Rule 12(b)(6) Mot. Dismiss (Defs.' Mot. Dismiss") [#25]. The motion is DENIED.

I. Facts

A. The ’820 Patent

The ’820 patent allows for the diagnosis of a form of Myasthenia Gravis, a chronic autoimmune disorder. U.S. Patent No. 7,267,820 col. 1 l. 13. Patients with Myasthenia Gravis experience waning muscle strength throughout the day, and symptoms include eye weakness (drooping eyelids, double vision), leg weakness, dysphagia (difficulty swallowing) and slurred or nasal speech. U.S. Patent No. 7,267,820 col. 1 l. 15-23. In 1960, it was discovered that in 80% of patients with Myasthenia Gravis, antibodies attack the acetyle choline receptor (AChR) (a neurotransmitter). In those patients, diagnosis is achieved through tests which detect the presence of AChR autoantibodies. U.S. Patent No. 7,267,820 col. 1 l. 34-36. Autoantibodies “are naturally occurring antibodies directed to an antigen which an individual’s immune response recognizes as foreign even though that antigen actually originated in the individual.” U.S. Patent No. 7,267,820 col. 1 l. 42-45. However, 20% of Myasthenia Gravis patients do not have the AChR autoantibodies despite experiencing the same symptoms and responding to the same therapies. U.S. Patent No. 7,267,820 col. 1 l. 36-40. For the 20% of Myasthenia Gravis patients who do not have the AChR autoantibodies, the ’820 patent inventors discovered that they had IgG antibodies that attack the N-terminal domains of muscle specific tyrosine kinase (“MuSK”), a receptor that is located on the surface of neuromuscular junctions. U.S. Patent No. 7,267,820 col. 1 l. 55-61.

The patent describes the method for a more accurate and speedy diagnosis of these patients. U.S. Patent No. 7,267,820 col. 3 l. 4-7. Specifically, the patent describes a method for diagnosing Myasthenia Gravis in which a radioactive label is attached to MuSK (or a fragment thereof) and is then introduced to a sample of bodily fluid. U.S. Patent No. 7,267,820 col. 3-4 l. 65-10. The method specifies that ^{125}I be used as the radioactive label. U.S. Patent No. 7,267,820

col. 4 l. 10. When ^{125}I-MuSK is introduced into the sample of bodily fluid, the MuSK autoantibodies, if present, attach to the labeled fragment. After the bodily fluid is immunoprecipitated, the presence of the radioactive label on any antibody indicates that the person is suffering from Myasthenia Gravis. U.S. Patent No. 7,267,820 col. 4 l. 8-10.

B. Infringement Allegations

Athena's test, FMUSK, uses the patented method to diagnose neurotransmission or developmental disorders related to MuSK. Compl. [#92 ¶ 16]; U.S. Patent No. 7,267,820, Claim 1. Plaintiffs allege that "Defendants, with specific knowledge of the '820 patent and the method it covers, surreptitiously and purposefully designed an alternate test to avoid paying Athena for Athena's licensed FMUSK test." Compl. [#92 ¶ 20]. Plaintiffs allege that Defendants availed themselves of the technology disclosed in the '820 patent, and developed two tests for diagnosing Myasthenia Gravis patients. Compl. [#92 ¶ 18]. Plaintiffs argue that Defendants' actions directly or indirectly, and literally or under the doctrine of equivalents, infringe the '820 patent. Compl. [#92 ¶ 24]. The claims at issue are those listed in claims 6-9 of the '820 patent. Pls.' Mem. Opp'n Defs.' Mot. Dismiss. 24 [#37]. Plaintiffs concede that they will not pursue infringement claims against Defendants based on the other claims in the patent. Pls.' Mem. Opp'n Defs.' Mot. Dismiss 8 [#37].

II. Motion to Dismiss

Defendants move to dismiss the complaint on the ground that the patent seeks to patent a law of nature, and it uses techniques standard in the art. Defs.' Mem. Supp. Mot. Dismiss 5 [#26]. Plaintiffs argue that the patent is not directed at a law of nature because the patent requires the production and use of ^{125}I-MuSK, a non-naturally occurring protein. Plaintiffs also argue that

applying various known types of procedures to a non-naturally occurring protein transforms the claim and makes it patent eligible. Pls.' Mem. Opp'n Defs.' Mot. Dismiss 14 [#37].

A. Standard of Review under 35 U.S.C. § 101

In applying § 101 at the pleading stage, the court construes the patent claims in a manner most favorable to the non-moving party. See Content Extraction & Transmission LLC v. Wells Fargo Bank, Nat'l Ass'n, 776 F.3d 1343, 1349 (Fed. Cir. 2014), cert. denied, 136 S. Ct. 119 (2015). As a threshold requirement for patent protection, the subject matter of a patent must be patentable under § 101; otherwise, the patent is invalid. Section 101 states "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. The Supreme Court has held that this section contains an implicit exception: "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." Alice Corp. Pty. Ltd. v. CLS Bank Intern., __ U.S. __, 134 S. Ct. 2347, 2354 (2014) (quoting Association for Molecular Pathology v. Myriad Genetics, Inc., __ U.S. __, 133 S. Ct. 2107, 2116 (2013)). Although "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas," these three patent-ineligible exceptions prevent "monopolization" of the "basic tools of scientific and technological work" and the impeding of innovation. Mayo Collaborative Servs. v. Prometheus Labs., Inc., __ U.S. __, 132 S. Ct. 1289, 1293 (2012).

To distinguish between patents that claim laws of nature, natural phenomena, and abstract ideas from patent-eligible inventions, the court must first determine whether the claims at issue are directed to one of those patent-ineligible concepts. Alice, 134 S. Ct. at 2355. If the concept is patent ineligible, the court then considers the elements of each claim both "individually and 'as

an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." Alice, 134 S. Ct. at 2355 (quoting Mayo, 132 S. Ct. at 1298, 1297). "We have described step two of this analysis as a search for an 'inventive concept' – i.e., an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" Alice, 134 S. Ct. at 2355 (quoting Mayo, 132 S. Ct. at 1294). At step two, more is required than well-understood, routine, conventional activity already engaged in by the scientific community. Rapid Litigation Management, Ltd. v. CellzDirect, Inc., __ F.3d __, 2016 WL 3606624, *3 (Fed. Cir. July 5, 2016).

B. Step One: Are Claims Directed to a Patent Ineligible Concept?

Defendants argue that the '820 patent is directed at a law of nature: that the bodily fluid of some people with Myasthenia Gravis have autoantibodies to MuSK. Plaintiffs argue that the patent method uses a man-made, patent eligible molecule, and uses that chemical complex in an innovative and transformative manner. Pls.' Surreply Opp'n Mot. Dismiss 4 [#46]. Per Plaintiffs, the claims are not directed to MuSK, instead, the claims "[r]ecite using a man-made chemically-modified version of MuSK to form a specific complex that does not occur in nature" and are therefore patent eligible. Pls.' Surreply Opp'n Mot. Dismiss 5 [#46].

The patent describes a method in which ^{125}I-MuSK is put into a sample of bodily fluid, and then the bodily fluid is filtered so that autoantibodies attached to the ^{125}I-MuSK are detected. The presence of the ^{125}I-MuSK autoantibodies indicates the person suffers from Myasthenia Gravis. The relevant portion of the patent states:

> The invention claimed is:
>
> **1.** A method for diagnosing neurotransmission or developmental disorders related to muscle specific tyrosine kinase (MuSK) in a mammal comprising the step of detecting in

a bodily fluid of said mammal autoantibodies to an epitope of muscle specific tyrosine kinase (MuSK).

2. A method according to claim 1 wherein said method comprises the steps of:
a) contacting said bodily fluid with muscle specific tyrosine kinase (MuSK) or an antigenic determinant thereof: and
b) detecting any antibody-antigen complexes formed between said receptor tyrosine kinase or an antigenic fragment thereof and antibodies present in said bodily fluid, wherein the presence of said complexes is indicative of said mammal suffering from said neurotransmission or development disorders.

3. A method according to Claim 2 wherein said antibody-antigen complex is detected using an anti-IgG antibody tagged or labeled with a reporter molecule.
. . .
6. A method according to claim 3 whereby the intensity of the signal from the anti-human IgG antibody is indicative of the relative amount of the anti-MuSK autoantibody in the bodily fluid when compared to a positive and negative control reading.

7. A method according to claim 1, comprising contacting MuSK or an epitope or antigenic determinant thereof having a suitable label thereon, with said bodily fluid, immunoprecipitating any antibody/MuSK complex or antibody/MuSK epitope or antigenic determinant complex from said bodily fluid and monitoring for said label on any of said antibody/MuSK complex or antibody/MuSK epitope or antigen determinant complex, wherein the presence of said label is indicative of said mammal is suffering from said neurotransmission or developmental disorder related to muscle specific tyrosine kinase (MuSK).

8. A method according to claim 7 wherein said label is a radioactive label.

9. A method according to claim 8 wherein said label is 125I.

U.S. Patent No. 7,267,820. Plaintiffs argue that because ^{125}I-MuSK is not naturally occurring, the claim is patent eligible under § 101. Pls.' Mem. Opp'n Defs.' Mot. Dismiss. 11 [#37] ("Those antibody/MuSK complexes are created in the laboratory and result from the use of a non-naturally-occurring laboratory-created molecule, ^{125}I-MuSK, and therefore, the antibody/MuSK complexes formed and detected by claim 9 are not found in nature.").

While ^{125}I-MuSK and the antibody/MuSK complexes are not found in nature, this does not transform the patent at issue here to a patent eligible concept. Contrary to Plaintiffs'

argument, the '820 patent is not a composition patent directed at the creation of the ^{125}I-MuSK auto-antibody complex. Rather, the patent is directed at a method for the diagnosis of a disease. U.S. Patent No. 7,267,820, col. 1 l. 9-11 ("The present invention is concerned with neurotransmission disorders and, in particular, with a method of diagnosing such disorders in mammals."). Although the patented method uses man-made ^{125}I-MuSK, the use of a man-made complex does not transform the subject matter of the patent. The focus of the claims of the invention is the interaction of the ^{125}I-MuSK and the bodily fluid, an interaction which is naturally occurring. The purpose of the patent is to detect whether any antibody-antigen complexes are formed between the ^{125}I-MuSK receptor and the antibodies "present in said bodily fluid." U.S. Patent No. 7,267,820, Claim 2. Counter to Plaintiffs' argument, because the patent focuses on this natural occurrence, it is directed to a patent-ineligible concept. See also Electric Power Group, LLC v. Alstom S.A., __ F.3d. __, 2016 WL 4073318, at *3 (Fed. Cir. Aug. 1, 2016) ("[W]e have described the first-stage inquiry as looking at the 'focus' of the claims, their 'character as a whole.'") (quoting Enfish, LLC v. Microsoft Corp., 822 F.3d 1327, 1335-36 (Fed. Cir. 2016)).

Athena's patent is similar to the patent invalidated by the Supreme Court in Mayo. In Mayo, the Supreme Court invalidated the patent of a diagnostic test which measured how well a person metabolized thiopurine drugs. 132 S. Ct. at 1295. The patent claimed a method in which the drug 6-thioguanine was given to a person, after which the level of 6-thioguanine in the person's blood stream was measured. Id. The Court held that the patent method was directed to observing a law of nature. "Prometheus' patents set forth laws of nature- namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of thiopurine drug will prove ineffective or cause harm." Id. at 1296. While the Court

acknowledged that it took human action (the administration of a thiopurine drug) to trigger the desired reaction, the reaction itself happened apart from any human action. Id. at 1297. The Court found the claim invalid because the method sought to measure how well a person metabolizes the drug. The Court described the interactions as 'entirely natural processes." Id. Likewise, Plaintiffs' method seeks to measure autoantibodies that have attached to a receptor protein, an interaction which is a similarly natural process. In Mayo, a man-made substance was administered to a person, and the by-product of the metabolization of that man-made substance was observed. Here, a man-made substance (^{125}I-MuSK) is administered to a sample of bodily fluid, and the by-product (^{125}I-MuSK autoantibodies) is observed. Mayo, 132 S. Ct. at 1297; see also Genetic Tech. Ltd. v. Merial LLC, 818 F.3d 1369, 1376 (Fed. Cir. 2016) (finding that when the patent claim focuses on a newly discovered fact about human biology, the claim is directed to unpatentable subject matter).

Further support can be found in Ariosa Diagnostics, Inc. v. Sequenom, Inc., 788 F.3d 1372 (Fed. Cir. 2015), cert. denied, 136 S. Ct. 2511 (2016). The case involved the patent for a method using fetal DNA for the diagnosis of certain conditions. The inventors discovered that cell-free fetal DNA ("cffDNA") was present in maternal plasma and serum. By implementing a method for detecting the small fraction of paternal cffDNA in the maternal plasma or serum, the inventors were able to determine certain inherited characteristics. Id. at 1373. The patent method isolated and amplified cffDNA, allowing for greater efficiency in diagnosis of genetic defects. As the court noted, "[t]he only subject matter new and useful as of the date of the application was the discovery of the presence of cffDNA in maternal plasma or serum . . ." Id. at 1377. Likewise, what is new and useful here is the discovery that some patients with Myasthenia Gravis have MuSK autoantibodies in their bodily fluid.

Relying on Rapid Litigation Mgmt. Ltd., 2016 WL 3606624 at *4, Plaintiffs seek to distinguish the '820 patent from Ariosa and Mayo by arguing that the '820 patent is focused on the steps required by the claimed method, rather than on the outcome of the diagnostic test. In Rapid Litigation Mgmt. Ltd., patent inventors discovered that hepatocytes, special liver cells that are used for testing, diagnostic, and treatment purposes, could be refrozen. Refreezing of hepatocytes was a breakthrough because the cells naturally have a short life span, and can only be harvested from a limited number of people. Prior to the discovery, hepatocytes could only be frozen one time, which limited their utility. Id. at *1. The patented method importantly allowed for multi-donor hepatocyte pools, a useful research tool that allows the study of a drug's impact on a representative population. Id. The Federal Circuit found the "end result of the '929 patent claims is not simply an observation or detection of the ability of hepatocytes to survive multiple freeze thaw cycles. Rather, the claims are directed to a new and useful method of preserving hepatocyte cells." Id. at * 4. The court found that the process' "desired outcome" was a method to produce something useful, and therefore was not directed at a patent ineligible concept. Id. The method allowed for refrozen hepatocyte cells to be used in a myriad of ways. Conversely, the desired outcome of the Plaintiffs' method is the detection of MuSK autoantibodies. It does not produce something useful beyond that diagnosis.

Plaintiffs' argument that the patent is transformed by the use of a man-made molecule is unavailing. The stated purpose of the patent is to diagnose Myasthenia Gravis, and the method is directed to a patent ineligible law of nature under § 101.

C. Step Two: Does the Inventiveness of the Claim make it Patent Eligible?

While the patent is directed to a patent ineligible concept under § 101, the patent can still be upheld if the method contains an "inventive concept." Alice, 134 S. Ct. at 2355.

Defendants argue that Plaintiffs' patent fails step two of § 101 analysis because it uses well-known techniques for identifying the presence of autoantibodies to MuSK and therefore does not contain an "inventive concept." Defs.' Mem. Supp. Mot. Dismiss 14 [#26] ("[P]rocess steps that recite techniques scientists would have already known to use in conjunction with the newfound natural law cannot supply the inventive concept."). Defendants cite to the patent specification which states that "[i]ondination and immunoprecipitation are standard techniques in the art, the details of which can be found in references (4 and 6)." Defs.' Mem. Supp. Mot. Dismiss 10 [#26]; U.S. Patent No. 7,267,820, col. 4, l. 9-12. Defendants note that the two publications referenced in the specification date from 1976 and 1985, and according to Defendants the publications describe "(1) the introduction of a ^{125}I-labeled antigen (AChR) into a bodily fluid sample, (2) immunoprecipitation, and (3) detecting the radioactive label." Defs.' Mem. Supp. Mot. Dismiss 10 [#26]. Defendants argue that the publications show that the methods described in the patent are commonly used by researchers in the field, and thus the claims do not pass step two of the analysis under § 101. Plaintiffs argue that a Rule 12(b)(6) motion cannot rely on extrinsic evidence to support the claim for dismissal, and that novelty and obviousness questions involve factual determinations that cannot be determined at the pleading stage. Pls.' Mem. Opp'n Mot. Dismiss 22 [#37].

The court cannot determine at this junction whether Plaintiffs' patented method uses standard techniques in the art, or whether it is sufficiently inventive to be patentable under the second step of Mayo. While it may later be established that the Plaintiffs' process is not deserving of patent protection because the techniques are standard in the art and therefore fail to provide an inventive concept, the court cannot resolve these factual determinations at the motion to dismiss stage. On the face of the claims and specification of the patent-in-suit, as well as on

the face of the complaint, the court cannot determine as a matter of law whether the patent provides a "combination of steps" to transform the method into a patent-eligible invention. Alice, 134 S. Ct. at 2360; see also, Mortgage Grader, Inc. v. First Choice Loan Services, Inc., 811 F.3d 1314, 1325 (Fed. Cir. 2016) ("Whether a claim is directed to statutory subject matter is a question of law. [D]etermination of this question may require findings of underlying facts specific to the particular subject matter and its mode of claiming[.]") (quoting Arrythmia Research Tech., Inc. v. Corazonix Corp., 958 F.2d 1053, 1055-56 (Fed. Cir. 1992)).

III. Conclusion

For the foregoing reasons, Defendants' Motion to Dismiss [#25] is DENIED.

August 25, 2016

/s/ Indira Talwani
United States District Court